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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,702	12/29/2005	Susanne Olausson	10400-000203/US	8760
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HARNESS, DICKEY & PIERCE, P.L.C. P.O.BOX 8910 RESTON, VA 20195			WANG, CHANG YU	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/562,702	OLAUSSON ET AL.
	<b>Examiner</b> Chang-Yu Wang	<b>Art Unit</b> 1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

1) Responsive to communication(s) filed on 20 April 2009.  
 2a) This action is FINAL.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

4) Claim(s) 57-61,71-83,93-101 and 103 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 57-61,71-83,93-101 and 103 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### **Priority under 35 U.S.C. § 119**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### **Attachment(s)**

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_  
 5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_

**DETAILED ACTION**

**RESPONSE TO AMENDMENT**

***Status of Application/Amendments/claims***

1. Applicant's amendment filed 4/20/09 is acknowledged. Claims 1-56, 62-70, 84-92, 102 and 104-112 are cancelled. Claims 57-61, 71-83, 93-101 and 103 are amended. Claims 57-61, 71-83, 93-101 and 103 are pending in this application and under examination in this office action.
2. Any objection or rejection of record, which is not expressly repeated in this office action has been overcome by Applicant's response.
3. Applicant's arguments filed on 4/20/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

***Claim Rejections/Objections Withdrawn***

4. The objection to claims 104-112 is moot because the claims are canceled. The objection to claims 57-103 is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 57-103 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 62-70, 84-92 and 102.

The rejection of claims 57-103 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 62-70, 84-92 and 102.

The rejection of claims 57-67, 71-74, 77-89, 93-97, and 100-103 under 35 U.S.C. 102 (b) as being anticipated by US Patent No. 6548569 (Williams et al. issued Apr 15, 2003, priority Mar 25, 1999.) as evidenced by US. Patent No. 5584885 (Seckel, issued on Dec 17, 1996) and Clavijo-Alvarez et al. (Plast. Reconstr. Surg. 2007. 119:1839-1851) is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 62-67, 84-89 and 102.

***Claim Rejections/Objections Maintained***

In view of the amendment filed on 4/20/09, the following rejections are maintained.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57-61, 71-83, 93-101 and 103 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6548569 (Williams et al., issued on Apr 15, 2003, priority date Mar 25, 1999) in view of US Patent No. 5656605 (Hansson et al., issued Aug 12, 1997) and US. Patent No. 5584885 (Seckel, issued on Dec 17, 1996). The rejection is maintained for the reasons made of record.

Claims 57-61, 82-83 and 100-101 as amended are drawn to a device/kit/biodegradable sheet for promoting regeneration of an injured nerve, comprising: a nerve encasement structure/biodegradable sheet/an dehydrate hydrogel and a plurality of biodegradable guiding fibers. The guiding fibers disclosed in the claimed device/kit/biodegradable sheet comprise polyhydroxybutyrate (PHB) and the PHB average molecular weight for the nerve encasement is within the range of 100,000-250,000daltons and the PHB average molecular weight for the guiding fiber is within the rang of 50,000 to  $\leq$  250,000 daltons wherein the guiding fibers have an in vivo degradation time (t1) that is less than tc, which is the required for establishing

regenerated contact between ends of an injured nerve using the device for regeneration and wherein  $t_1 < 14 + L/v$  and  $L/v \leq t_0 \leq 14 + L/v$  and wherein "L" is the nerve gap (mm) of the injured nerve and "v" is the axon growth rate (mm/day) of the injured nerve, typically 0.5-2mm/day. The nerve encasement structure has an in vivo degradation time ( $t_2$ ) that is longer than  $t_1$ . The  $t_2$  is also longer than  $t_r$ , which is the time required for the entire nerve regeneration process to be completed, and wherein  $t_2 > t_1$ ;  $t_2 > 2(L/v)$ ; and  $2(L/v) \leq t_r \leq 14 + 2(L/v)$ .

Dependent claims are directed to as follows: the nerve encasement structure comprises a compressed non-woven sheet with a unidirectional fiber orientation (claims 71, 93) and the guiding units comprise a non-bonded fiber web with a unidirectional fiber orientation (claims 72, 94). Furthermore, the device/kit/sheet further comprises a dehydrate hydrogel matrix (claims 73, 95-96), an active substance or cell (claims 74-77, 97-99 and 103). Moreover, the guiding units occupy  $\leq 2.0\%$  by volume of the lumen formed by the nerve encasement structure (claim 77), the cross-section dimension of the guiding units is  $\leq 50\mu\text{m}$  (claim 78),  $\leq 20\mu\text{m}$  (claim 79),  $5-15\mu\text{m}$  (claim 80).

On p. 19-21 of the response, Applicant argues that the cited references do not render the claimed invention obvious because the cited referenced provides no suggestion that a material of low molecular weight degrading more quickly than the corresponding material of high molecular weight under identical conditions. Applicant argues that Williams only teaches the molecular weight of PHB used for a nerve guide

may be chosen from 10,000 to 10,000,000 Daltons. Applicant further cites Jansen et al. (Biomaterials. 2004, 25: 483-489) in support of the arguments.

In contrast to Applicant's arguments, the cited references do render the claimed device obvious. Williams teaches a biodegradable device comprising poly-4-hydroxybutyrate (PHB) (see col.7, lines 31-33, in particular) in a form of porous conduit such as having the shape of the nerve conduit products of NEUROTUBE<sup>TM</sup> as incorporated by the references including US Patent NOS. 5735863, 5584885 and 5026381. The device disclosed by Williams meets the limitation of "the device comprising a nerve encasement structure and a plurality of biodegradable guiding units as recited in the independent claims because the shape of the NEUROTUBE is a nerve encasement structure and the PHB polymers encompassed within the encasement structure are fabricated into fibers, sheets, foams, coating structures, filaments, which are a plurality of biodegradable guiding fibers as recited in the independent claims (see col. 16, lines 42-52; col. 25, line 50-col. 28, lines 35, in particular). The molecular weight of PHB polymer is between 300 to 10<sup>7</sup> Daltons, and the preferred embodiment is 10,000 to 10,000,000 Daltons (see col. 6, lines 6-10). Williams teaches formation of PHB microspheres with the size of 1-10 $\mu$ m (see col. 39, example 12, in particular), which meets the limitation of " the cross-section dimension of the guiding fibers is  $\leq$ 50 $\mu$ m,  $\leq$ 20 $\mu$ m or 5-15 $\mu$ m as recited in instant claims 78-80.

As previously made of record, the instant specification only describes a conduit made from a non-woven sheet of polyhydroxybutyrate (PHB) having a molecular weight of 140,000, a sheet thickness of 0.25mm and a weight per unit area of 10mg/cm<sup>2</sup> and

filled with non-bonded PHB fibers with an average molecular weight of 80,000 and cross-sectional dimensions within the range of 5-15 $\mu$ m wherein the conduit is able to repair a 10mm gap of an injured sciatic nerve. Since the structures and compositions of the nerve guides or devices disclosed by Williams are the same as those described in the specification and the range of the molecular weight of PHB overlaps with the claimed range, the prior art would also have the same properties of t1, t2, tc and tr as recited in independent claims.

Williams also teaches that degradation rate of the PHB polymer in the nerve guide or biodegradable device is manipulated through addition of components to the polymeric composition, selection of the chemical composition of the polyhydroxyalkanoate polymer through selection of monomeric units, as chemical linkages, which are incorporated into the polymer, by alteration of the linkages, chemical backbone or pendant groups, molecular weight, processing conditions, or form of the composition, and wherein the polyhydroxyalkanoate polymer has an average molecular weight of between 10,000 and 10,000,000 Dalton; and wherein the form of the composition refers to the porousness and surface area of the composition (see col. 10, lines 6-col. 12, line 22; col. 33-35, examples 4-5; col. 37-39, examples 6-11; col. 39, lines 41-46, in particular). Thus, Williams does teach that changing the molecular weight of the guiding fibers and the nerve encasement structure can change the degradation rate of guiding fibers and the nerve encasement. In addition, Williams teaches a spinal fusion device fabricated from PHB to improve the degeneration disc diseases (see col. 20, line 50-col. 21, line 52; col. 35-36, tables 6-7, in particular).

Although Williams does not explicitly teach that the average molecular weight of PHB is within the range of 100,000 to 250,000 Daltons for the nerve encasement and does not teach that is within the range of 50,000 to <250,000 for the guiding fibers, Williams teaches that PHB polymers have an average molecular weight of between 10,000 and 10,000,000 Dalton (see col. 39-40, claim 1; col. 10, lines 6-col. 12, line 22; col. 33-35, examples 4-5; col. 37-39, examples 6-11; col. 39, lines 41-46, in particular). Williams also teaches that the units of PHB polymers are 10-100,000 and preferably 100-30,000 units and that the molecular weight of the PHB polymers for biodegradable devices is between 10,000-10,000,000 Dalton (see col. 5, lines 40-col. 6, line 10; col. 39, claim 1, in particular). Williams also teaches that the device comprising PHB polymers can be coated or fabricated to medical device to improve their compatibility, tailoring their degradation and controlled release profiles (see col. 27, lines 1-35, in particular). Thus, it is obvious to modify the molecular weight of PHB to alter and make the degradation rate of the guiding fibers is less than that of the never encasement structure in the biodegradable device (such as a Neurotube) as disclosed by Williams because Williams teaches the range of 10,000 and 10,000,000 Daltons for the PHB in the Neurotube and also teaches alteration of the molecular weight of PHB in the Neurotube or nerve guide can change the degradation rate of the Neurotube or the nerve guide.

Note that

In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990), See MPEP 2144.05-I

\*a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties.

*Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)" See MPEP 2144.05-I

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105USPQ 233, 235 (CCPA 1955)" See MPEP 2144.05-II

***Conclusion***

6. NO CLAIM IS ALLOWED.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/  
Chang-Yu Wang, Ph.D.  
August 5, 2009

/Christine J Saoud/  
Primary Examiner, Art Unit 1647